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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,057	01/28/2004	Roy H. Larsen	50147/003002	2306

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,057	LARSEN ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1,2,7,8,13,14,16-18-21,23, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1 and 7 recites the broad recitation antibody or antibodies, and the claim also recites "preferably of IgG or IgM class" which is the narrower statement of the range/limitation.

4. Regarding claim 1, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05 (d).

5. In claim 1, the phrase "folate derivatives" is indefinite because it is not clear what all is encompasses thereby. The term is not defined in the specification, nor it this an art recognized term. Since there would be an unlimited number of ways that folate could be derivatized, the scope of this term cannot be ascertained and therefore is indefinite.

6. Regarding claim 7, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05 (d).

7. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the various method steps required to prepare the conjugate, i.e. conjugating folate to an antibody, radiolabelling the conjugate, etc. The claim as presented is a method claim, but does not include any actual steps of preparation.

8. Also, in claim 7, the recitation of "standard procedures" is indefinite. The specification does not define what is encompassed by standard procedures and "standard procedures" is not an art-recognized term, given that there are various divergent procedures in the art for radiolabelling. Thus is it unclear what is meant by "standard procedures: and the scope thereof cannot be determined.

9. In claim 8, the recitation of "fragment or construct" (3 recitations) is indefinite because it is not clear what it is a fragment or construct of. This rejection can be obliviated by inserting "thereof" after these phrases to show it is a fragment of construct of an antibody.

10. Claim 13 recites "polyclonal antibody from other species" are derived from different cell lines from multiple species. It is not determined which polyclonal antibody is claimed from which cell line or species.

11. Claim 14 and 18-20 recites the limitation "the flolate binding protein" in line 3. There is insufficient antecedent basis for this limitation in the claim.

12. Claims 16, 17 and 21 provide for the use of a folate-antibody-radionuclide conjugate, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practice.

13. Claim 24 recites the limitation "the dual-binding-ability principle" in line 2. There is insufficient antecedent basis for this limitation in the claim. Further, it is unclear what is meant by "the dual-binding-ability principle" as this is neither an art-recognized term nor is this principle defined by the specification.

14. Claim 24 recites the limitation "the active component" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

15. Regarding claim 24, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP §2173.05(d).

16. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the various method steps required to prepare the pharmaceutical solution. The claim as presented is a method claim, but does not recite any actual steps of preparation.

Claim Rejections - 35 USC § 101

17. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16,17,21 and 24 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Sinkule et al. (EP 282057).

20. Sinkule et al. (EP 282057) teaches of a receptor binding conjugate comprising three components, 1.) an antibody, 2.) a radionuclide and 3.) a chemotherapeutic agent, such as folate or analogues thereof (abstract; p 2,column 2, lines 29-30). The antibody may be a monoclonal or polyclonal or variations thereof used for a wide variety of target antigens (p 3, column 1, lines 56+; column 4, lines 9-12). Methods of making conjugates, using linkers, etc. are set forth on p 5-7. Various radionuclides are disclosed, such as ^{125}I or others listed in the instant claims (p 3, column 1, lines 39+). The therapeutic agent chosen for use will vary according to the nature of the disease to be treated and the type of target cells to be eradicated *in vivo* within human or mammalian host (column 3, lines 5-12; column 5, lines 22-25). The conjugate can be administered by any conventional method, such as intravenously and the pharmaceutical agents may be in various pharmaceutical compositions with various combinations of materials therefore, which would encompass the kits, as claimed (column 6, lines 48+).

21. Claims 1,7,8,14,16-21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Niswender et al (US 4,336,185).

22. Niswender (US 4,336,185) teaches of a receptor binding conjugate comprising three components, 1.) an antibody (e.g. gamma globulin, aka, immunoglobulin), 2.) a radionuclide or radionuclides and 3.) folic acid and salts, esters, and amides thereof (abstract, column 1, lines 3-6). Methods of making the conjugates are disclosed in column 2-3).

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claim1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (US 6,077,499) in view of Goldenberg et al. (US 5,698,178).

25. Griffiths et al. (US 6,077,499) discloses a receptor binding conjugate comprising a targeting moiety (e.g. an antibody or fragment thereof), one or more therapeutic agents and folic acid derivatives where the therapeutic agents may be a radionuclide or mixtures thereof (abstract; column 10; column 8, line 48; column 3, line 36). Various antibodies, fragments, hybrids etc. thereof may be employed (column 5-6) as well as

methods of making the conjugates are disclosed as set forth in the examples. Griffiths et al. (US 6,077,499) does not disclose that the conjugates may be prepared in kits having separate container/vials or the use of all the same antibodies as the instant claims, e.g. humanized antibodies.

26. Goldenberg et al. (US 5,698,178) discloses receptor binding conjugates which comprise various antibodies and at least one diagnostic or therapeutic agent (abstract, column 4, lines 20). The diagnostic and therapeutic agents include radionuclides and folic acid analogues (column 23, lines 11+; line 57). Humanized antibodies may be used as an equivalent to other antibodies for targeting a desired site and that the use of humanized antibodies obviates potential problems associated with the immunogenicity of murine constant regions (column 10, line 17+; column 12, lines 4-13).

27. At the time of the invention it would have been obvious to one ordinarily skilled in the art to modify the conjugates, methods of making and kits thereof disclosed by Griffiths to use a type of antibody, such as humanized antibodies because Griffiths teaches that various types of antibodies and related forms may be used as equivalents to impart a desired targeting function and the use of humanized antibodies for targeting is well known in the art and provides the advantage of obviating potential problems associated with the immunogenicity of murine constant regions, as shown by Goldenberg.

Double Patenting

28. Claims 1-7 and 15-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. US 6,740,304 B2) in view of Sinkule et al. (EP 282057). The instant claims disclose a radiopharmaceutical receptor binding conjugate comprising folate, antibody and radionuclide and its use as a pharmaceutical by injecting into humans a suitable solution. The method of administration is for the delivery of potentially therapeutic radiation to malignant cells, such as brain, lung, etc. The exact method of delivery of therapeutic radiation comprising an antibody, folate, and radionuclide for binding to malignant cells, such as brain, lung, etc. is disclosed in US 6,740,304 B2 as well as the radionuclides (^{125}I) of the instant claims.

Conclusion

No claims are allowed at this time. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
June 19, 2006

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER